## TRPC3 and GLUT4 interact during insulin-mediated glucose uptake in adult skeletal muscle

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We examined the role of the $Ca^{2+}$ permeable canonical transient receptor potential 3 (TRPC3) channels in insulin-mediated glucose uptake in skeletal muscle. Adult male mice were killed by rapid neck disarticulation and the hindlimb flexor digitorum brevis (FDB) muscles were removed. The study was approved by the Stockholm North local ethical committee. Intact, single muscle cells were isolated from the FDB muscles and TRPC3 was knocked down with siRNA, which was introduced into the cells with a novel transfection technique involving carbon nanotubes. TRPC3 expression in siRNA treated cells was decreased by ~40% and this was accompanied by ~80% decrease in insulin-meidated glucose uptake. TRPC3 can be directly activated by diacylglycerol (DAG) and knock down of TRPC3 inhibited DAG-induced $Ca^{2+}$ influx. TRPC3 was detected in GLUT4 immunoprecipitates. Immunofluorescence staining showed a clear overlap between TRPC3 and GLUT4 in the proximity of the t-tubular system, which is the major site of insulin-mediated glucose uptake in skeletal muscle. In conclusion, TRPC3 functionally and physically interacts with GLUT4 in skeletal muscle and $Ca^{2+}$ influx through TRPC3 has a large impact on the insulin-mediated glucose uptake.